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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,191	09/21/2005	Daniela Bundschuh	26967U	7383

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
08/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,191	BUNDSCHUH ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-19 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The term "close in time" in claims **9-12 and 19** is a relative term which renders the claim indefinite. The term "close" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The term "in any order whatever to a patient in need thereof " in claims **9-11** renders the claims vague and indefinite. It is not clear what the applicant meant by such term.

Claims **12-18** are rejected for depending on a rejected base claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 2, 4-6, 9-10, 12-15 and 18-19 are rejected under 35 U.S.C. 102(e) as being anticipated by Knowles et al (WO 03011274).

Knowles et al teach formulations and method of treating pulmonary diseases such as obstructive pulmonary disease or asthma by administering a PDE4 inhibitor in combination with an anticholinergic agent (see abstract). The PDE4 inhibitor useful in this invention may be any compound that is known to inhibit the PDE4 enzyme and used in treating inflammation and as bronchodilators (see page 3). Preferred PDE4 inhibitors include roflumilast and preferred anticholinergics include ipratropium bromide, oxitropium bromide and tiotropium bromide (see pages 4-5). The said compounds can be formulated for **oral** administration such as tablets, syrups, etc or for **inhalation** (see page 6).

Knowles et al disclose that both active agents would be administered at the same time, or very close in time, or one drug could be taken in the morning and one later in the day (see page 7, lines 27-32). Medicament packs containing an effective amount of

both medications for treating respiratory disorders or reducing the symptoms of a pulmonary disorder are disclosed (see page 2, lines 14-36).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 7-8, 11 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knowles et al (WO 03011274).

Knowles et al, discussed above, teaches that the medicaments can be administered in dosage forms such as oral, nasal, dermal or inhalation but lacks disclosure on intravenous. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have hosen intravenous as one of the

suitable dosage forms because intravenous administration is well known in the art and provides fast onset of action. In other words selecting intravenous route instead of oral is a simple substitution and leads to predictable results.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeadon et al (WO 02096463) in view of Keller et al (6,585,958).

Yeadon et al ('463) teach a PDE4 inhibitor and anti-cholinergic agent in combination for treating obstructive airway disorders. It is disclosed that a combination of a selective PDE4 inhibitor and an anti-cholinergic agent offers significant benefits in the treatment of obstructive airways and other inflammatory diseases over treatment with either agent alone. The advantage of the combination is to provide optimal control of airway caliber through the mechanism most appropriate to the disease pathology, namely muscarinic receptor antagonism, together with effective suppression of inappropriate inflammation. By administering a combination of an anticholinergic agent and a selective PDE4 inhibitor via the inhaled route, the benefits of each class are realized without the unwanted peripheral effects. Further, the combination results in unexpected synergy, producing greater efficacy than maximally tolerated doses of either class of agent used alone (see page 3).

Yeadon et al ('463) also discloses an inhaled combination of a selective PDE4 inhibitor and an anticholinergic agent for simultaneous, sequential or separate administration (see page 4). The preferred ratio, by weight of selective PDE4

inhibitor:anticholinergic agent used will depend on the particular combination being examined.

Yeadon et al discloses suitable PDE4 inhibitors and suitable anti-cholinergics. Anti-cholinergics include ipratropium and oxitropium (see pages 6-10). The combinations of the said therapeutic agents are useful in the treatment of atopic and non-atopic asthma and COPD or COAD (see page 12). Yeadon et al ('463) lacks specific disclosure on the combination of roflumilast and tiotropium bromide.

Keller et al teach medicinal aerosol formulations comprising one or more pharmaceutically active agents. Suitable agents include anticholinergics such as ipratropium bromide, oxitropium bromide and tiotropium bromide. Suitable leukotriene antagonists include roflumilast (see column 8). The formulations can be in the form of a solution or suspension (see col. 9, lines 38-48).

It would have been obvious to one of ordinary skill in the art at the time the invention was made given the formulations comprising a combination of a PDE4 inhibitor and an anti-cholinergic agent of Yeadon et al ('463) to have looked in the art for specific PDE4 agents and anti-cholinergic agents suitable for treating respiratory disorders such as COPD and asthma, as taught by Keller et al with the reasonable expectations of successfully treating patients that need such treatments. Although Yeadon et al and Keller et al do not specifically teach administration of one of the active agents by oral or intravenous routes, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have selected a different, but well

known route of administration and provide more choices for the patient or health provider.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeadon et al (WO 02096423).

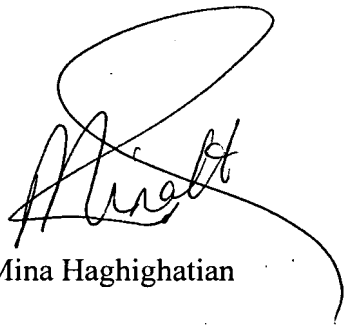
Yeadon et al ('423) teaches combination of a PDE4 inhibitor and tiotropium or derivatives thereof for treating obstructive airways and other inflammatory diseases. Yeadon et al discloses that suitable PDE4 inhibitors including roflumilast (see pages 13-14). Anti-cholinergic agents include ipratropium and oxitropium as well as tiotropium bromide (see pages 29-30). The formulations are packaged for insertion into a device capable of simultaneous or sequential delivery.

Although Yeadon et al does not teach administration of active compounds by any route other than inhalation, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the dosage forms because oral and intravenous dosage forms and routes of administrations are well known in the art and one of ordinary skill in the art would have been able to choose the dosage form suitable for the specific treatment. In other words this is a simple substitution of one known route of administration for another known rout of administration, which would yield predictable results.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mina Haghighatian

Patent Examiner

July 31, 2007